

WHAT IS CLAIMED IS

1. A pharmaceutical composition for reducing oxidative damage or delaying senescence comprising an orally administrable effective unit dosage of a primary N-hydroxylamine or a pharmaceutically acceptable salt thereof and substantially free of a nitrone corresponding to 5 the hydroxylamine, wherein the hydroxylamine has the general formula,



wherein R_1 , R_2 and R_3 are independently selected from: hydrogen, substituted or unsubstituted (C1-C10) alkyl, alkenyl, alkynyl, aryl, oxyl, acyl, carboxyl, amino, nitro, nitroso, oxime, hydrazone, azo, thiol, sulfonyl and halide.

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2. A composition according to claim 1, wherein the dosage is from 100ug to 1g.

3. A composition according to claim 1, wherein at least one R of R_1 , R_2 and R_3 is selected from unsubstituted (C1-C10) alkyl, alkenyl and alkynyl.

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4. A composition according to claim 1, wherein at least one R of R_1 , R_2 and R_3 is selected from unsubstituted (C1-C18) alkyl, cycloalkyl, alkenyl and alkynyl, and the R is selected from: $\text{CH}_3\text{-(CH}_2\text{)}_{n1}$, $(\text{CH}_3\text{-(CH}_2\text{)}_{n2}\text{-})_2\text{CH}$, $(\text{CH}_3\text{-(CH}_2\text{)}_{n2}\text{-})_3$, cyclopentyl, cyclohexyl, $(\text{CH}_2\text{=CH-CH}_2\text{)}_{n3}$ and $(\text{CH}=\text{C-CH}_2\text{-})_{n3}$, wherein $n1 = 1$ to 18, $n2 = 1$ to 17 and $n3 = 1$ to 3.

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5. A composition according to claim 1, wherein at least one R of R_1 , R_2 and R_3 is selected from hydrogen, unsubstituted (C1-C10) alkyl, alkenyl and alkynyl, and the hydroxylamine is selected from:

N-methylhydroxylamine,
N-ethylhydroxylamine,
N-n-propylhydroxylamine,
N-(n-butyl) hydroxylamine,
5 N-(n-pentyl)hydroxylamine,
N-(n-hexyl)hydroxylamine,
N-(n-heptyl)hydroxylamine,
N-(n-octyl)hydroxylamine,
N-(n-nonyl)hydroxylamine,
10 N-(n-decyl)hydroxylamine,
N-(n-dodecyl)hydroxylamine,
N-(n-decahexyl)hydroxylamine,
N-(n-decaoctyl)hydroxylamine,
N-isopropylhydroxylamine,
N-sec-butylhydroxylamine,
N-tert-butylhydroxylamine,
N-cyclohexylhydroxylamine,
N-cyclopentylhydroxylamine,
N-(2-propene)hydroxylamine,
N-(3-butene)hydroxylamine,
N-(2-propyne)hydroxylamine and
N-(3-butyne)hydroxylamine.

6. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted aryl.

15 7. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted aryl, and the R is selected from: mono, di, or tri methyl, methoxy, halo, nitro, amino, hydroxyl and substituted or unsubstituted phenyl, naphthyl, anthryl, phenanthryl, pyridyl, quinolinyl, imidazolyl, benzoxazolyl, pyrrolyl, furanyl, piperidinolyl and tetrahydrofuranolyl.

20 8. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted aryl, and the hydroxylamine is selected from:

N-benzylhydroxylamine, N-(1,3-diaminobenzyl)hydroxylamine,
25 N-(n-nitrobenzyl)hydroxylamine, N-(1,3-hydroxybenzyl)hydroxylamine,
N-(n-methylbenzyl)hydroxylamine, N-(2,4-diaminobenzyl)hydroxylamine,
N-(n-chlorobenzyl)hydroxylamine, N-(2,4-dihydroxybenzyl)hydroxylamine,
N-(n-aminobenzyl)hydroxylamine, Imidazole-2-methylhydroxylamine and
N-(n-hydroxybenzyl)hydroxylamine, Benzoxazole-2-methylhydroxylamine,

30 wherein n is selected from 1, 2, 3, 4, 5 and 6.

9. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is substituted

or unsubstituted (C1-C18) oxyl.

10. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) oxyl and the R is selected from: hydroxyl, 5 hydroxyalkyl (HO-(CH₂)_{n1}), hydroxyaryl selected from benzylalcohol, phenol and naphthol, alkoxy (O-(CH₂)_{n1}) and aryloxy selected from phenoxy, benzyloxy and naphthyoxy, wherein n1= 1 to 18.

11. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18)alkyl hydroxyl or arylhydroxyl and the hydroxylamine 10 is selected from:

N-(hydroxymethyl)hydroxylamine,	N-(methoxymethyl)hydroxylamine,
N-(2-hydroxyethyl)hydroxylamine,	N-(methoxyethyl)hydroxylamine,
N-(3-hydroxypropyl)hydroxylamine,	N-(methoxyisopropyl)hydroxylamine,
15 N-(4-hydroxybutyl)hydroxylamine,	N-(benzyloxymethyl)hydroxylamine and
N-(6-hydroxyhexyl)hydroxylamine,	N-(4-hydroxymethylbenzyl)hydroxylamine.
N-(12-hydroxydodecyl)hydroxylamine,	

12. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) alkylcarboxyl or arylcarboxyl.

20 13. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) alkyl or aryl carboxyl and the R is selected from carboxyalkyls and benzyl.

25 14. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted alkyl (C1-C18) or arylcarboxyl and the hydroxylamine is selected from:

N-(carboxymethyl)hydroxylamine,	N-(5-carboxypentyl) hydroxylamine,
30 N-(2-carboxyethyl)hydroxylamine,	N-(6-carboxyhexyl)hydroxylamine,
N-(3-carboxypropyl)hydroxylamine,	N-(4-carboxybenzyl)hydroxylamine and
N-(4-carboxybutyl)hydroxylamine,	N-(12-carboxydodecyl)hydroxylamine.

15. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) ester.

5 16. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) ester and the R is selected from alkyl (C1 – C18) and aryl esters.

10 17. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted alkyl (C1-C18) or arylesters and the hydroxylamine is selected from:

N-(acetyloxymethyl)hydroxylamine,
N-(acetoxyethyl)hydroxylamine,
N-(acetoxypropyl)hydroxylamine,
N-(propylcarbonyloxy)methylhydroxylamine,
15 N-(butylcarboxyloxy)methylhydroxylamine,
N-(tert-butyloxycarboxyl)methylhydroxylamine,
N-(benzyloxycarbonyl)methylhydroxylamine,
N-(phenyloxycarbonyl)methylhydroxylamine,
N-(3-pyridyloxycarbonyl)methylhydroxylamine and
20 N-(benzoxazol-5-carbonyloxy)methylhydroxylamine.

18. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) carbonyl.

25 19. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted carbonyl and the R is selected from alkyl (C1 – C18) carbonyls and aryl carbonyls.

30 20. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted alkyl (C1-C18) or arylcarbonyls and the hydroxylamine is selected from:

N-(acetyl)methylhydroxylamine,
N-(ethylcarbonyl)methylhydroxylamine,
N-(butylcarbonyl)methylhydroxylamine,
N-(phenylcarbonyl)methylhydroxylamine
and
N-(benzylcarbonyl)methylhydroxylamine.

5 21. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is
substituted or unsubstituted alkyl(C1-C18) or aryl amino.

10 22. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is
substituted or unsubstituted alkyl (C1-C18) or aryl amino and the R is selected from primary
alkyl amine selected from methylamine, ethylamine, propylamine, butylamine and
hexylamine, secondary amine selected from dimethylamine, diethylamine and dipropylamine,
tertiary amine selected from trimethyl and triethylamine, and quarternary amine selected from
tetramethyl and tetra-ethylammonium salts.

15 23. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is
substituted or unsubstituted alkyl(C1-C18) or aryl amine and the hydroxylamine is selected
from:
N-aminomethylhydroxylamine,
N-(2-aminoethyl)hydroxylamine,
N-(N-methylamino)methylhydroxylamine,
N-(N,N-dimethylamino)methylhydroxylamine,
N-(N,N,N-trimethylammonium)methylhydroxylamine,
N-(3-aminopropyl)hydroxylamine,
N-(6-aminohexyl)hydroxylamine,
N-(4-aminobenzyl)hydroxylamine,
25 Hydroxylamine-1-methylpyridinium and
Hydroxylamine-1-methylquinolinium.

30 24. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is
substituted or unsubstituted (C1-C18) alkyl or aryl nitro.

35 25. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is

substituted or unsubstituted alkyl(C1-C18) or aryl nitro and the R is selected from alkynitro selected from nitromethyl, nitroethyl, nitropropyl, nitrobutyl, nitropentyl, nitrohexyl and nitrobenzyl, and arylnitro selected from nitrophenyl and nitronaphthyl.

5 26. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted alkyl (C1-C18) or aryl nitro and the hydroxylamine is selected from:

N-(nitromethyl)hydroxylamine,	N-(5-nitropentyl)hydroxylamine,
N-(2-nitroethyl)hydroxylamine,	N-(6-nitrohexyl)hydroxylamine,
10 N-(3-nitropropyl)hydroxylamine,	N-(4-nitrobenzyl)hydroxylamine and
N-(4-nitrobutyl)hydroxylamine,	N-(2,4-dinitrobenzyl)hydroxylamine.

27. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) nitroso.

15 28. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) nitroso and the R is selected from aliphatic nitrosoamines and aromatic nitroso.

20 29. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted nitroso (C1-C18) and the hydroxylamine is selected from:
N-(N-methyl-N-nitroso-amino)methyl hydroxylamine,
N-(N-methyl-N-nitroso-2-amino)ethylhydroxylamine,
N-(N-methyl-N-nitroso-3-amino)propylhydroxylamine and
25 N-(p-nitroso)benzylhydroxylamine.

30. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted oxime.

30 31. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) oxime and the R is selected from: acetaldoxime, propionaldoxime, butanaldoxime and benzaldoxime.

32. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted oxime (C1-C18) and the hydroxylamine is selected from:
Acetaldoxime-3-hydroxylamine, Butanaldoxime-5-hydroxylamine and
Propionaldoxime-4-hydroxylamine, (4-benzaldoxime)1-methylhydroxylamine.

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33. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C10) hydrazone.

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34. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C10) hydrazone and the R is selected from: acetaldehyde hydrazone, propanaldehyde hydrazone, butanaldehyde hydrazone and phenylhydrazone.

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35. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted hydrazone (C1-C10) and the hydroxylamine is selected from
1-hydroxylamine-acetaldehyde hydrazone, 1-hydroxylamine-butanaldehyde hydrazone
1-hydroxylamine-propanaldehyde and
hydrazone, 1-hydroxylamine-benzylaldehyde
hydrazone.

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36. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted azo.

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37. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted azo and the R is selected from: azobenzene, p-(phenylazo)benzyl and p-diazobenzyl.

38. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted azo and the hydroxylamine is selected from:
N-(p-phenylazo)benzylhydroxylamine,
N-(p-diazobenzyl)hydroxylamine and
N-(p-methoxylphenylazo)benzylhydroxylamine

39. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) thiol.

40. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) thiol and the R is selected from (C1-C18) alkylthiol selected from methyl, ethyl, propyl, butyl, pentyl and hexyl thiol, and arylthiol selected from thiophenol and benzylthiol.

41. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) thiol and the hydroxylamine is selected from:

N-(thiomethyl)hydroxylamine, N-(3-thiopropyl)hydroxylamine and
N-(2-thioethyl)hydroxylamine, N-(p-sulphydryl)benzylhydroxylamine.

42. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) sulfonic acid.

43. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) sulfonic acid and the R is selected from methanesulfonic acid, ethanesulfonic acid, propanesulfonic acid, butanesulfonic acid and p-toluenesulfonic acid.

44. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) sulfonic acid and the hydroxylamine is selected from:

1-hydroxylamine-methanesulfonic acid,
1-hydroxylamine-ethane-2-sulfonic acid,
1-hydroxylamine-propane-3-sulfonic acid,
1-hydroxylamine-butane-4-sulfonic acid
and
N-(p-sulfobenzyl)hydroxylamine.

45. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is halide.

46. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is halide and the R is selected from F, Cl, Br and I.

47. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is halide and the hydroxylamine is selected from:

N-(chloromethyl)hydroxylamine, N-(4-chlorobutyl)hydroxylamine,
N-(bromomethyl)hydroxylamine, N-(p-chlorobenzyl)hydroxylamine,
5 N-(2-chloroethyl)hydroxylamine, N-(p-fluorobenzyl)hydroxylamine and
N-(3-chloropropyl)hydroxylamine, N-(p-iodobenzyl)hydroxylamine.

48. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted hydroxylamine.

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49. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted hydroxylamine and R is selected from N-methylhydroxylamine, N-ethylhydroxylamine, N-propylhydroxylamine N-butylhydroxylamine, N-pentylhydroxylamine, and N-benzylhydroxylamine.

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50. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted hydroxylamine and the hydroxylamine is selected from:

Bis-methylhydroxylamine, Bis-(3-propyl)hydroxylamine and
Bis-(2-ethyl)hydroxylamine, Bis-benzylhydroxylamine.

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51. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) phosphoester.

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52. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) phosphoester and the R is selected from: dimethylphosphate, diethylphosphate, dipropylphosphate and benzylphosphate.

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53. A composition according to claim 1, wherein at least one R of R₁, R₂ and R₃ is substituted or unsubstituted (C1-C18) phosphoester and the hydroxylamine is selected from: di-hydroxylaminemethylphosphate ester, mono-hydroxylaminemethylphosphate ester, mono-(1-hydroxylamine)-ethyl-2-phosphate ester,

di-(1-hydroxylamine)-2-ethylphosphate ester,
di-(1-hydroxylamine)-3-propyl-phosphate ester,
mono-(hydroxylamine-benzyl-phosphate ester and
di-hydroxylamine-benzylphosphateester.

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54. A composition according to claim 1, wherein the nitrone is less than 1% (wt/wt) of the hydroxylamine in the composition.

10 55. A composition according to claim 1 further comprising an effective amount of a

carnitine.

56. A method for reducing oxidative damage to, or delaying senescence of a cell comprising the step of contacting a cell subject to or at risk of undesirable oxidative damage or senescence with a composition according to claim 1.

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57. A method for reducing oxidative damage to, or delaying senescence of a cell comprising the steps of:

identifying a cell as subject to or at risk of undesirable oxidative damage or senescence; and

20 contacting the cell with a composition according to claim 1.

58. A method according to claim 57, wherein the cell is contained in other than a cancerous host.